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Peculiarities of Redox State in Thalassemic Red and White Blood Cells. The Effects of Antioxidants and Iron Chelators.

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It is well established that patients suffering from β -thalassemia are subjected to *in vivo* oxidative stress. The crucial role of loose "free" iron bound to the membrane of β -thalassemic erythrocytes in the generation of hydroxyl radicals with subsequent oxidation of membrane lipids and proteins has also been shown. On these grounds, the application of iron chelators as essential part of the conventional therapy of iron-overloaded thalassemic patients is thought to be relevant both in terms of iron removal from the body and the amelioration of ROS levels. Unfortunately, chelating therapy is associated with a number of adverse effects such as immunodepression, impairment of vision and audibility, vascular complication, etc. Safe and effective agents capable of improving both the genetically associated and chelator-induced clinical conditions of thalassemic patients are of great importance. Some antioxidants in combination with iron chelators and fetal hemoglobin inducers could be considered for lifelong management of β -thalassemia. This study was designed to compare the peculiarities of ROS production/utilisation by circulating red (RBC) and white (WBC) blood cells of patients with different severity of β -thalassemia (*major*, *intermedia*, and *minor*) and to elucidate the effects of some non-toxic antioxidants and immunomodulators in these processes. Among antioxidants, flavonoid rutin, lipoic acid, N-acetylcystein, and Bio-Normalizer (a functional food with definite immuno- and redox-modulating activities produced by the yeast and microbial fermentation of unripe papaya fruits) were thoroughly investigated. We found features of substantial oxidative stress in RBC and oxidative deficiency in WBC: both redox disorders depended on the clinical form of disease. While oxidative stress appears to be a causative reason for the excessive RBC destruction, oxidative deficiency may account for the increased susceptibility to infections and vaso-occlusive complications. Desferal taken at the low concentrations revealed significant pro-oxidant effect towards both RBC and WBC. Pro-oxidant action of chelator was transformed to antioxidant one at its higher concentrations. Noteworthy that the chelator-induced ROS overproduction by WBC was mainly observed intracellularly. In our opinion, sharp increase in ROS formation may lead to the "suicidal" WBC damage and, as a result, to the chelator-induced leukopenia. Contrary to our expectations, the antioxidants lipoic acid and NAC aggravated to some extent the state of oxidative stress in RBC although by different mechanisms. At the same time, rutin protected RBCs and WBCs against endogenous and exogenous oxidative damage but did not improve the state of oxidative deficiency in WBC. The best effects on the redox status in RBC and WBC were observed in the presence of Bio-Normalizer. To prove the efficacy of this food additive, proper clinical trials should be performed.